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| EXAMINER | |
|---|---|
| CHUI, MEI PING | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/542,495 | BAULIEU ET AL. | |
| | Examiner | Art Unit | |
| | MEI-PING CHUI | 1616 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-8 and 11-13* is/are pending in the application.

4a) Of the above claim(s) *7,11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 8, 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *n/a*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/06/2009 has been entered.

### *Status of Action*

Receipt of Amendments/Remarks filed on 11/06/2009 is acknowledged. Claims 1-8, 11-13 are pending in this application. Claims 9-10 have been previously cancelled; claims 1, 3-5 and 8 have been currently amended; new claim 13 is added.

Receipt of Declaration of 37 CFR 1.132 filed on 11/06/2009 is acknowledged.

Upon further consideration, the Examiner has new grounds of rejection presented in this Office Action.

### *Priority*

Acknowledgment is made of Applicants' claim for foreign priority based on an application filed in France on 01/17/2003. However, it is noted that Applicants have not filed a certified copy of the English translation of the foreign application No. 03/00507 as required by 35 U.S.C. 119(b).

### *Status of Claims*

Accordingly, claims **1-6, 8 and 13** are presented for examination on the merits for patentability as they read upon the elected subject matter and claims 7 and 11-12 directed

to non-elected invention are withdrawn.

Rejections and/or objections not reiterated from the previous Office Action are hereby withdrawn. The following rejection(s) is/are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

***Claim Rejections - 35 USC § 112 first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

***Scope of Enablement of the Invention***

Claims 1-6, 8 and 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Firstly, claim 1 while being enabling for treating an acute or chronic lesion, or a degenerative disease of the nervous system by administering the compounds: 3β-methoxy-pregna-5-ene-20-one (3-methoxy-PREG), 3β-methoxy-pregna-5-ene-20-one-17α-dichloromethyl and 3β-methoxy-5α-pregnane-20-one, it does not reasonably provide enablement for the treatment by administering the compounds: 3β-methoxy-pregna-5,14-diene-20-one, 3β-methoxy-PREG-16α, 17α-epoxy and 3β-methoxy-PREG-16α, 17α-methylene. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claim.

Secondly, claim 2 while being enabling for treating medullary compression and Alzheimer's disease, does not reasonably provide enablement for treating Parkinson's disease, aged-induced memory loss, memory loss induced by the taking of substances, a traumatic lesion, a cerebral lesion, a lesion of spinal cord, pain, notably neuritic pain, nerve degeneration and multiple sclerosis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claim.

An analysis of whether the scope of a particular claim is actually supported by the disclosure in a patent application requires a determination of whether the disclosure, at the time of filing, contained sufficient information regarding the subject matter of the claim at issue so as to enable one skilled in the pertained art to use the claimed invention without undue experimentation. *In re Wands*, 8 USPQ 2d 140 (Fed. Cir. 1988). Therefore, the test of enablement is not whether experimentation is necessary, but rather, if experimentation is in fact necessary, whether it is reasonably considered to be undue. *In re Angstadt*, 190 USPQ 214, 219 (CCPA 1976). Determining the issue of enablement with respect to a claim is a question of law based on underlying factual findings. *In re Vaeck*, 20 USPQ 2d, 1444 (Fed. Cir. 1991). More particularly, there are many factors to be considered in determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, and whether any necessary experimentation is reasonably considered to be "undue". See *In re Wands* at page

1404. MPEP § 2164.01(a). The court in *In re Wands* set forth the following factors to be considered, which included, without limitation, the: 1). scope or breadth of the claims; 2). nature of the invention; 3). relative level of skill possessed by one of ordinary skill in the art; 4). state of, or the amount of knowledge in, the prior art; 5). level or degree of predictability, or a lack thereof, in the art; 6). amount of guidance or direction provided by the inventor; 7). presence or absence of working examples; and 8). quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

Scope or breadth of the claim:

(1) Claim 1 is broader in scope than the enabling disclosure. The specification merely discloses, without more, the compounds: 3β-methoxy-pregna-5, 14-diene-20-one; 3β-methoxy-PREG-16α,17α-epoxy and 3β-methoxy-PREG-16α,17α-methylene, which are derived from PREG-16α,17α-epoxy and PREG-16α,17α-methylene, are effective to stimulate the polymerization of microtubules induced by MAP2 and to stimulate neuritic sprouting. However, Applicants are claiming utilizing any of the claimed compounds can effectively treat an acute or chronic lesion, or a degenerative disease of the nervous system, even though the stimulation of neuritic sprouting produced by these compounds: 3β-methoxy-pregna-5, 14-diene-20-one; 3β-methoxy-PREG-16α,17α-epoxy; and 3β-methoxy-PREG-16α,17α-methylene (based on the results of PREG-16α,17α-epoxy and PREG-16α,17α-methylene) are lower than that produced by pregnenolone (the control) (see Specification: page 21-22, Example 10).

(2) Claim 2 is also broader in scope than the enabling disclosure for the diseases that can be effectively treated by the compound, i.e. 3β-methoxy-pregna-5-ene-20-one (3-methoxy-PREG), as claimed. The specification merely discloses, without more, the treatment results for the diseases, i.e. medullary compression and Alzheimer's disease. However, Applicants are claiming utilizing the claimed compound also can effectively treat Parkinson's disease, aged-induced memory loss, memory loss induced by the taking of substances, a traumatic lesion, a cerebral lesion, a lesion of spinal cord, pain, notably neuritic pain, nerve degeneration and multiple sclerosis, even though some of these diseases, i.e. multiple sclerosis or pain, are known to derive from various origins, cause and mechanisms.

Nature of the invention:

The nature of the invention is directed to a method of treating an acute, or chronic lesion, or a degenerative disease of the nervous system, i.e. medullary compression, Alzheimer's disease, Parkinson's disease, aged-induced memory loss, memory loss induced by the taking of substances, a traumatic lesion, a cerebral lesion, a lesion of spinal cord, pain, notably neuritic pain, nerve degeneration and multiple sclerosis, by administering to a patient of a composition, which comprises 3β-methoxy-pregna-5-ene-20-one (3-methoxy-PREG: represented by the structure set forth above) or the formula I derived from pregnenolone that contains a 3-methoxy function, as set forth above.

State of or the amount of knowledge in the prior art:

It is known in the art that the cause of multiple sclerosis is unknown and researchers are still not sure what triggers an attack to patients with multiple sclerosis except there

appears to be a genetic link to this disease (see www.nlm.nih.gov/medlineplus/ency/article/000737.htm, MedlinePlus Medical Encyclopedia Multiple Sclerosis, dated on 08/06/2007, Page 1-2). It is also known that multiple sclerosis appears to affect woman more than man, and people with a family of multiple sclerosis and those who live in a geographical area with a higher incidence rate for multiple sclerosis have a higher risk of the disease (MedlinePlus Medical Encyclopedia: Multiple Sclerosis, page 2; also see WebMD: Multiple Sclerosis – Prevention, via www.webmd.com/multiple-sclerosis/tc/multiple-sclerosis-ms-prevention, dated on 03/23/2006). Therefore, currently there is no known method that can cure disease, i.e. multiple sclerosis, because the causes of this disease is still unknown and the occurrence of this disease is derived from diverse factors.

Amount of guidance or direction provided by the inventor, and presence or absence of working examples:

Although the instant specification discloses that the compound 3β-methoxy-pregna-5-ene-20-one (3-methoxy-PREG) is effective for treating medullary compression and Alzheimer's disease, it remains silent on the effectiveness for treating these diseases provided by other claimed compounds, i.e. the compounds of formula I. Likewise, the specification is also silent on the effectiveness for treating the diseases, i.e. Parkinson's disease, aged-induced memory loss, memory loss induced by the taking of substances, a traumatic lesion, a cerebral lesion, a lesion of spinal cord, pain, notably neuritic pain, nerve degeneration and multiple sclerosis, utilizing the compounds, i.e. 3β-methoxy-pregna-5-ene-20-one (3-methoxy-PREG and the compounds of formula I, as claimed.

The specification provides some results and working embodiments with respect to the administration of the compound: 3β-methoxy-pregna-5-ene-20-one (3-methoxy-PREG) for treating medullary compression and Alzheimer's disease, as well as the stimulation of neuritic sprouting. However, in the specification, there is no example(s) for the administration of other claimed compounds, and there is no example(s) for the treatment of other diseases, i.e. multiple sclerosis, pain or neuritic pain, as claimed in the instant invention.

Level or degree of predictability, or a lack thereof, in the art:

A high degree of unpredictability exists in the state of the art regarding how to treat multiple sclerosis and pain because, at this stage of the art, the causes and mechanism of multiple sclerosis, pain including neuritic pain, are still unknown and the factors that may trigger these diseases still cannot be controlled, such as the factors due to the potential of weak immune system or the gene that one inherits from their parents, or other unknown promoting factors.

In particular, a high degree of unpredictability, not to mention a great deal of uncertainty and limitation of current pain, including neuropathic pain, drugs, existed in the state of the prior art regarding the aspects of bioavailability, toxicity, dose-related symptoms and adverse effects that all may limit the ability to titrate drugs up to efficacious doses. Since such limitations existed in the relevant research field related to the instant invention that requiring each embodiment of the invention to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that

the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue.

Further, their mode of action is often unknown or very unpredictable and administration of the claimed compounds can be accompanied by undesirable side effects such as additive or antagonistic effect as opposed to synergism. Thus, in the absence of a showing of correlation between all the pain and neuropathic pain types claimed as capable of being treated by the claimed compounds of the instant claims, one of ordinary skill in the art is unable to fully predict possible results from the administration of the compounds: 3β-methoxy-pregna-5-ene-20-one (3-methoxy-PREG) or the formula I, due to the unpredictability of the role of the huge number of pain types can be encompassed in the manner as claimed (see: CMAJ, 2006: August, 175(3), 265-275 and PNAS, 1999, 96, 12905-12910).

The quantity of experimentation needed is undue because one of ordinary skill in the art would first need to determine the types of pain or neuropathic pain to be treated, and then determine which claimed compounds: 3β-methoxy-pregna-5-ene-20-one (3-methoxy-PREG) or the formula I would be effective for the treatment of those types of pain, , with no assurance of success.

Quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure:

One of ordinary skill in the art would be required to conduct an undue amount of experimentation to reasonably and accurately determine whether the claimed compounds and corresponding method of the instant application does in fact effectively treat all the

claimed acute, or chronic lesion, or degenerative disease of the nervous system in the instant invention.

In conclusion, it is readily apparent from the aforementioned disclosure, in conjunction with a corresponding lack of scientific data and working embodiments regarding the claimed compounds of formula I and the claimed diseases, i.e. Parkinson's disease, aged-induced memory loss, memory loss induced by the taking of substances, a traumatic lesion, a cerebral lesion, a lesion of spinal cord, pain, notably neuritic pain, nerve degeneration and multiple sclerosis; claims 1-6, 8 and 13 are not enabled because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

For these reasons, Applicants are required to provide additional guidance and direction with respect to how to use the claimed subject matter in claims 1-6, 8 and 13 in order for the application to be to the full scope of the claimed invention.

***Claim Rejections - 35 USC § 112 second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. All dependent claims are included in this rejection.

Firstly, claim 2 is rejected because the claim is written using improper Markush format "wherein said disease or lesion is **selected from the group comprising** Alzheimer's disease, Parkinson's disease..." (see claim 2, line 2). Although alternative claim expressions using Markush format are permitted, they must present no uncertainty or ambiguity with respect to the question of scope or clarity of the claim. It is suggested that the phrase "**selected from the group consisting of...and...**" be adopted.

In addition, claim 2 recites a broad limitation together with a narrow limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 2 recites the broad recitation where the acute or chronic lesion or a degenerative disease of the nervous system is selected from the group consisting of "Alzheimer's disease, Parkinson's disease...a cerebral lesion, a lesion of the spinal cord", and the claim also recites "**in particular** medullary compression, ischemia, pain...and multiple sclerosis", which is the narrower statement of the limitation.

Furthermore, claim 2 recites the term "notably" which renders the claim indefinite.

The term "notably" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In the instance case, it is unclear as to what level of pain intensity is considered "notably" and what level is not.

***Claim Rejection - 35 U.S.C. § 102***

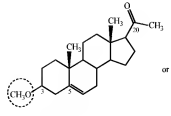
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102(a) that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless:

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

**Claims 1-6, 8 and 13 are rejected under 35 U.S.C. 102(a) as being anticipated by Baulieu et al. (EP 1310258).**

Instant claims are drawn to a method of treating an acute, or chronic lesion, or a degenerative disease of the nervous system, comprising the administration to a patient of a composition, which comprises 3β-methoxy-pregna-5-ene-20-one (3-methoxy-PREG: represented by the structure as follows) or the formula I (represented by the structure as follows) derived from pregnenolone that contains a 3-methoxy function.



3β-methoxy-pregne-5-ene-20-one or the formula I (i.e. 3β-methoxy-5α-pregnane-20-one) ;

wherein the composition is administered by injection or orally, and the acute or chronic

lesion, or degenerative disease of the nervous system is not ischemia.

The prior art Baulieu et al. disclose a method for the enhancement of memory and cognitive functions by administering tot he individual a therapeutically effect amount of an enantiomer of a steroid, wherein the individual has suffered memory loss resulting from a cause of age, i.e. normal-age related memory loss or dementia; neurological disorders, neuro-psychiatric disorders, i.e. anxiety, chronic stress, depression, sleep disturbance, drug related memory loss; neurodegenerative disorders, i.e. Alzheimer's disease; and amnesia resulting, i.e. from an injury or other trauma (page 3: [0010-0014, 0016]; page 5: [0027]).

Baulieu et al. also disclose that the suitable steroid enantiomer, i.e. 3β-methoxy-pregna-5-ene-20-one or 3β-methoxy-pregnane-20-one, can be used (page 4: [0017], line 7, 14), and wherein the typical administered dosage of the steroid enantiomer fall within the range of from about 0.1 to about 5 mg/kg of a patient's weight, or preferably about 1 mg/kg of a patient's weight (page 5: [0032]). It is noted that the dosage discloses by Baulieu et al. can be calculated corresponding to 7-350 mg or, preferably, 70 mg per an average 70 kg body weight.

Baulieu et al. further disclose that the composition also comprises a pharmaceutically acceptable carrier or excipient, and the composition can be administered by parenterally, i.e. injection, or orally (page 5: [0030], line 1-6, 10; page 6: column 9, line 3, Example 3 for treatment and injection procedure).

With respect to the limitation where the composition is administered to the patient in an amount effective to stimulate polymerization and/or stabilization of microtubules in the patient, it is noted that Baulieu et al. disclose the steroid 3β-methoxy-pregna-5-ene-20-one and 3β-methoxy-pregnane-20-one, which are identical to the compounds as claimed. Since

a chemical compound and its properties are inseparable. Therefore, if the prior art discloses the identical chemical structure, the properties applicant discloses and/or claims are necessarily present (see MPEP 2112.01: Part II and also see *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

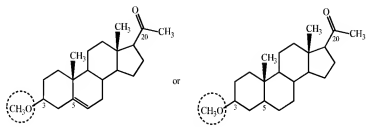
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

**(1) Claims 1-6 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chopp et al. (U. S. Patent No. 6,245,757).**

***Applicants Claim***

Applicants claim a method of treating an acute, or chronic lesion, or a degenerative disease of the nervous system, comprising the administration to a patient of a composition, which comprises 3β-methoxy-pregna-5-ene-20-one (3-methoxy-PREG: represented by the

structure as follows) or the formula I (represented by the structure as follows) derived from pregnenolone that contains a 3-methoxy function:




3β-methoxy-pregne-5-ene-20-one the formula I (i.e. 3β-methoxy-5α-pregnane-20-one) ;

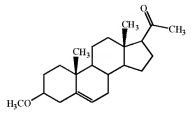
wherein the composition is administered by injection or orally.

***Determination of the scope and content of the prior art***

***(MPEP 2141.01)***

Chopp et al. teach a method for the treatment of ischemic damage, i.e. damage due to stroke, comprising administering to a mammal afflicted with ischemic cell damage an effective amount of a pharmaceutical composition comprising progestin and a pharmaceutically acceptable delivery vehicle (see Abstract and column 2, lines 28-45). Chopp et al. also teach that the method functions by the ability of the progestin or its derivative to reduce the damage caused by ischemia, i.e. brain damage caused by cerebral ischemia, and the significant neurological functions improvement, as well as the enhancement of the ability of the brain to recognize after damage, be enhancing its intrinsic ability to compensate for injury (column 2, lines 38-45). As a result, the method provides whereby ischemic tissue, including tissue of the central nervous system or muscle tissue, can be treated so as to improve tissue survival and to hasten general bodily recovery (column 4, lines 22-26).

Chopp et al. then teach that the useful progestin or its derivatives for the treatment, which includes pregnenolone and pregnenolone methyl ether represented by the structure as follows (column 4, line 58; column 5, lines 4-5):



pregnenolone methyl ether

Chopp et al. further teach that the progestin or its derivatives can be formulated as pharmaceutical formulations and administered to a mammal, i.e. human patient, in a variety of unit dosage forms, i.e. injection, adapted to the chosen route of administration, i.e. orally or parenterally includes intravenous route (column 5, lines 55-60 ad column 6, line 43). For oral administration, the progestin can combine with or more pharmaceutical excipients, so that the progestin is formulated to pass through the blood-brain barrier and enters the central nervous system at widespread sites and can effectively reduce infarct size following acute, focal ischemia, i.e. middle cerebral artery occlusion, when given before and after the onset of ischemia (column 6, lines 1-2; column 12, Example 2: lines 9-11; column 3, lines 63-67; column 4, line 1 and column 5, line 4).

In addition, Chopp et al. teach that each unit dosage form comprises the active progestin in amounts from 5-1000 mg (column 7, lines 14-17). Therefore, it meets the limitation of the compound 3-methoxy-PREG and the amounts ranging from 50 to 2500 mg" as claimed.

With respect to the recitation of the types of disease, i.e. an acute lesion, memory loss induced by a traumatic lesion, a cerebral lesion, ischemia, as claimed in claim 1 and

claim 2, Chopp et al. teach that the treatment method utilizes the progestin or its derivatives for reducing ischemic damage due to stroke or myocardial infarction (see Abstract), wherein the treatable ischemia can be resulted from brain damage caused by cerebral ischemia (column 2, lines 38-41 and column 4, lines 9-12) or can be trauma resulting from ischemic insult (column 4, lines 13-20). It is also known that stroke is a type of acute ischemia and is commonly referred as brain ischemia or acute ischemic stroke. Therefore, the teaching of Chopp et al. meets the recitation of "an acute lesion" in claim 1 and the recitation of "a traumatic lesion", "a cerebral lesion" and "ischemia", as claimed in claim 2.

With respect to the recitation of "wherein the drug also comprises an excipient that makes it possible to formulate...." in claim 3 is an optional claim language (see MPEP 2106 (II)). Further, Applicants broadly claim "an excipient" without any structural limitation. Therefore, the examiner takes the position that any excipient taught in the prior art reads on the limitation of claim 3 for the reason set forth above, since the prior art excipient and the claimed excipient are not structurally distinguishable. In order to be limiting, the intended use must create a structural difference between the claimed composition and the prior art composition. In the instant case, the intended use does not create a structural difference, thus the intended use is not limiting.

With respect to the limitation where the composition is administered to the patient in an amount effective to stimulate polymerization and/or stabilization of microtubules in the patient, it is noted that Chopp et al. teach the steroid pregnenolone methyl ether, which is identical to the compound 3-methoxy-PREG, as claimed. Since a chemical compound and its properties are inseparable. Therefore, if the prior art discloses the identical chemical

structure, the properties applicant discloses and/or claims are necessarily present (see MPEP 2112.01: Part II and also see *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

***Ascertainment of the difference between the prior art and the claims***

***(MPEP 2141.02)***

Chopp et al. do not use the compound pregnenolone methyl ether in the examples. However, Chopp et al. suggest that pregnenolone methyl ether as one of the useful progestin derivative that can be used for treating ischemic damage.

***Finding of prima facie obviousness Rational and Motivation***

***(MPEP 2142-2143)***

It would have been obvious to a person of ordinary skilled in the art at the time the invention was made to follow the guidance of Chopp et al. to arrive at the instant invention.

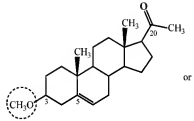
One of ordinary skill would have been motivated to try and choose one of the desirable progestin or its derivative, i.e. pregnenolone methyl ether, for reducing the brain damage caused by ischemia, for improving the neurological functions and for enhancing the ability of the brain to recognize after damage and its intrinsic ability to compensate for injury because the prior art suggested for doing so.

From the teaching of the reference, one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

**(2) Claims 1-6, 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stein et al. (U. S. Patent No. 2002/0072509).**

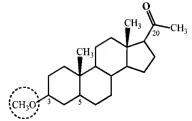
***Applicants Claim***

Applicants claim a method of treating an acute, or chronic lesion, or a degenerative disease of the nervous system, comprising the administration to a patient of a composition, which comprises 3β-methoxy-pregna-5-ene-20-one (3-methoxy-PREG: represented by the structure as follows) or the formula I (represented by the structure as follows) derived from pregnenolone that contains a 3-methoxy function:




3β-methoxy-pregne-5-ene-20-one

or




the formula I (i.e. 3β-methoxy-5α-pregnane-20-one) ;

wherein the composition is administered by injection or orally.

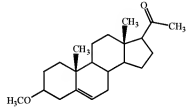
***Determination of the scope and content of the prior art***

***(MPEP 2141.01)***

Stein et al. teach a method and a composition for the treatment of neuro-degeneration following a traumatic injury to the central nervous system by reducing, or eliminating, neuronal cell death, edema, ischemia, and enhancing tissue viability, such that the treatment can enhance survival, proliferation, or/and neurite outgrowth of the neurons that either prevents or retards neuro-degeneration, i.e. a progressive loss of neurons in the central nervous system (page 2: [0016], lines 1-8). Stein et al. teach that the physiological

events lead to the neuro-degeneration of the CNS tissues following a traumatic CNS injury, i.e. cerebral edema, increase in the immune and inflammatory response, demyelinization (page 2: [0017], lines 1-6).

Stein et al. also teach that the neuro-protective method is achieved by the administration of a therapeutically effective composition comprising a progestin or a progestin derivative to a patient, i.e. human; wherein the useful progestin or its derivative, i.e. pregnenolone methyl ether as represented by the structure below, can be used (page 2: [0018], lines 26-27 and 40):




pregnenolone methyl ether

Stein et al. further teach that the composition may further comprise a pharmaceutically acceptable carrier vehicle, and the composition can be prepared into a pharmaceutically useful composition suitable for all forms of dose administration, i.e. injection and oral. Stein et al. teach that due to the traumatic CNS injury, the blood brain barrier may be more permeable for allowing the active compound to enter the cerebral spinal fluid (page 5: [0036-0037] and [0039-0041]).

With respect to the suitable amount of progestin in a dose, Stein et al. teach that such amount can be varied from about 1 μg to about 50 mg per kg of average body weight for the

administration to a patient (which corresponds to about 14 mg to about 3500 mg per 70 kg of average body weight) (page 5: [0036-0037] and [0039-0041]).

With respect to the limitation where the composition is administered to the patient in an amount effective to stimulate polymerization and/or stabilization of microtubules in the patient, it is noted that Stein et al. teach the steroid pregnenolone methyl ether, which is identical to the compound 3-methoxy-PREG, as claimed. Since a chemical compound and its properties are inseparable. Therefore, if the prior art discloses the identical chemical structure, the properties applicant discloses and/or claims are necessarily present (see MPEP 2112.01: Part II and also see *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

***Ascertainment of the difference between the prior art and the claims***

***(MPEP 2141.02)***

Stein et al. do not use the compound pregnenolone methyl ether in the examples. However, Stein et al. suggest that pregnenolone methyl ether can be used as one of the useful progestin for protecting neuro-degeneration following a traumatic injury and enhance survival, proliferation, or/and neurite outgrowth of the neurons that either prevents or retards neuro-degeneration.

***Finding of prima facie obviousness Rational and Motivation***
***(MPEP 2142-2143)***

It would have been obvious to a person of ordinary skilled in the art at the time the invention was made to follow the guidance of Stein et al. to arrive at the instant invention.

One of ordinary skill would have been motivated to try and choose one of the desirable progestin or its derivative, i.e. pregnenolone methyl ether, for reducing the brain damage caused by ischemia, for improving the neurological functions and for enhancing the ability of the brain to recognize after damage and its intrinsic ability to compensate for injury because the prior art suggested for doing so.

From the teaching of the references, one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

***Response to Arguments***

Applicants' arguments filed on 11/06/2009 have been considered but are not persuasive.

Applicants argue that *Chopp's* and *Stein's* classification of pregnenolone methyl ether as a progestin, i.e. having progesterone activity was incorrect. This is, in part, because 3-methoxy-PREG is modified to prevent it from being converted into progesterone (or its active metabolites) *in vivo*. In addition, the purported therapeutic effects of progestins reported in *Chopp* and *Stein* were due to their progesterone activity. 3-methoxy-PREG, however, lacks this progesterone activity and even antagonizes it. In fact, the purportedly therapeutic progestins used in *Chopp* and *Stein* lack the microtubule stabilizing activity required by Applicant's methods and as recited in Applicant's claims (Remarks: page 7-8).

The arguments are not persuasive because both prior arts Chopp et al. and Stein et al. teach the compositions that can be utilized to treat neuro-degeneration caused by traumatic

injury to the central nervous system. The ultimate goal of their treatment methods is to reduce neuronal cell death and to enhance tissue viability, such that the treatment can enhance survival, proliferation, and/or neurite outgrowth of the neurons that retards progressive loss of neurons in the central nervous system. Chopp et al. and Stein et al. also suggest a list of progestins and progestin **derivatives** including the claimed compound pregnenolone methyl ether (3-methoxy-PREG), which can be used to treat the neuro-degenerative disorders as set forth above. Since both prior art Chopp et al. (U. S. Patent No. 6,245,757) and Stein et al. (U. S. Patent Application Publication No. 2002/0072509) are published references and are available to the public; one of ordinary skill in the art would have been motivated to follow the teaching of the prior art by trying the compounds from the list and choose the desirable one for use in the method, as claimed for treating an acute or chronic lesion, or a neurodegenerative diseases, as the treatment methods taught by both prior art, namely Chopp et al. and Stein et al.

With respect to the limitation where the composition is administered to the patient in an amount effective to stimulate polymerization and/or stabilization of microtubules in the patient, it is noted that both Chopp et al. and Stein et al. teach the steroid **pregnenolone methyl ether**, which is identical to the claimed compound 3-methoxy-PREG, and the **effective amount** as claimed. Since a chemical compound and its properties are inseparable. Therefore, if the prior art discloses the identical chemical structure, the properties applicant discloses and/or claims are necessarily present (see MPEP 2112.01: Part II and also see *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

***Response to Declaration of 37 CFR 1.132***

Applicants' submission of Declaration of 37 CFR 1.132 filed on 11/06/2009 has been considered but is not persuasive.

The declaration is not persuasive because the evidence of non-obviousness was not commensurate in scope with the claim invention and the evidence was not side-by-side comparison with the closest prior art.

In the instance case, Applicants provided evidence to show that progesterone and the claimed 3-methoxy-PREG possess different progesterone receptor activities, in which the former (progesterone) is a progesterone receptor agonist and the latter (3-methoxy-PREG) is a progesterone receptor antagonist (see Declaration: Exhibit F). However, the instant invention: first, requires the claimed compound, i.e. 3-methoxy-PREG, to be capable of stimulate polymerization and/or stabilization of microtubules in the patient. Secondly, the instant specification uses pregnenolone as a control to determine the effectiveness of the claimed compounds to stimulate polymerization and/or stabilization of microtubules and stimulate neuritic sprouting (se Specification: page 22). It is noted that both compounds: pregnenolone and 3-methoxy-PREG (pregnenolone methyl ether) are taught by the prior art Chopp et al. and Stein et al. for utilizing in methods of treating neuro-degeneration diseases to the central nervous system to reduce neuronal cell death and to enhance survival, proliferation, and/or neurite outgrowth of the neurons. Therefore, Applicants merely showing 3-methoxy-PREG possesses different progesterone receptor activity as opposed to progesterone is not a sufficient evidence to overcome the nonobviousness because the evidence was not commensurate in scope with the claim invention.

***Conclusion***

No claims are allowed.

***Contact Information***

Any inquiry concerning this communication from the Examiner should direct to Helen Mei-Ping Chui whose telephone number is 571-272-9078. The examiner can normally be reached on Monday-Thursday (7:30 am – 5:00 pm). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where the application or proceeding is assigned is 571-273-8300.

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/H. C./

Examiner, Art Unit 1616

*/Mina Haghighatian/*
Primary Examiner, Art Unit 1616